Women's health from a global economic perspective

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CHAPTER 3

Cost-effectiveness of scaling up modern family planning interventions in low- and middle-income countries: an economic modeling analysis in Indonesia and Uganda

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Submitted

ABSTRACT

Objectives: To estimate the long-term cost-effectiveness of improved family planning interventions to reduce the unmet need in L-MICs, with Indonesia and Uganda as reference cases.

Methods: The analysis was performed using a Markov decision analytic model, where current situation and several scenarios to reduce the unmet need were incorporated as the comparative strategies. Country-specific evidences were synthesized from the Demographic and Health Survey (DHS) and published studies. The model simulated the natural history of sexual and reproductive health experience of women in the reproductive age over a lifetime time horizon. Modeled outcomes included clinical events, costs and incremental cost-effectiveness ratios expressed as cost per disability adjusted life year averted (ICERs per DALY). Deterministic and probabilistic sensitivity analyses were conducted to assess the impact of parameter uncertainty on modeled outcomes.

Results: In the hypothetical cohort of 100,000 women, scenarios to reduce the unmet need for family planning would result in savings within a range of US$ 230,600 - US$ 895,100 and US$564,400 - US$1,865,900 in Indonesia and Uganda, respectively. The interventions would avert an estimated 1,859 - 3,780 and 3,705 - 12,230 DALYs in Indonesia and Uganda, respectively. The results of our analysis indicate that scaling up family planning dominates the current situation in all scenarios in both countries, with lower costs and fewer DALYs. These results were robust in sensitivity analyses.

Conclusion: Scaling up family planning interventions could improve women's health outcomes substantially and be cost-effective or even cost-saving across a range of scenarios compared to the current situation.

INTRODUCTION

Unmet need for family planning (FP) is still a relevant issue in many countries, despite the global increase in FP in the last 20 years[1]. According to World Health Organization (WHO), women with unmet need are defined as those who desire to either cease or delay conception, but are not using any method of contraception. Unmet FP need and numbers of unintended pregnancies are especially high in low and middle income countries (L-MICs), which consequently further contribute to rapid population growth in these regions[1,2]. Unmet FP needs are also responsible for approximately 7.4 million disability-adjusted life years (DALYs) and considerable maternity-related disease burden[3,4].

FP is one of the four core strategies of the Safe Motherhood Initiative - besides antenatal care, safe delivery, and postnatal care - to improve maternal health and to reduce the number of maternal deaths[5]. Unmet need for modern FP, the increasing trends in this need as well as the expected growth in the number of potential contraceptive users in L-MICs indicate that increased investment in FP interventions that improve access to the full range of affordable high-quality contraceptives and its related services is essential in order to meet the demand[1]. The current use of contraceptives is estimated to prevent 272,040 maternal deaths and satisfying the unmet need could reduce the number with another 104,000 deaths annually[2]. Over the last decade, several global initiatives to increase women's access to modern FP methods in L-MICs have been implemented by addressing policies, financing, supply, service delivery and socio-cultural barriers. A recent review indicates that improving FP in L-MICs appears to be cost effective; however, this evidence is supported by a limited amount of studies only, with varying quality and outcomes, hampering comparability. Therefore, further studies are needed to generate more comprehensive assessments on costs and cost-effectiveness to potentially support increased attention, funding, and investments in FP programs[6].

We adopted a decision analytic framework to assess the long-term cost-effectiveness of scaling up FP interventions to reduce the unmet need for FP. The present evaluation concerns case studies for Indonesia and Uganda to represent a middle-income country with a moderate and stagnant level of unmet need and a low-income country with a relatively high level of unmet need, respectively. Notably, varying levels of contraceptive prevalence, unmet need and cost effectiveness thresholds in these countries allow the analysis to contrast both costs and health consequences of the intervention over a range of settings as illustrated by these two distinct countries.

METHODS

Model overview

A Markov decision analytic model was developed to analyze cost, health outcomes, and cost-effectiveness of interventions to increase the use of modern FP methods, compared to the current situation in Indonesia and Uganda. Notably, in our analysis, the term FP concerns modern family planning methods. In accordance with data from the Demographic and Health Survey (DHS), we categorized oral contraceptives, intrauterine devices, injectables, implants, condoms, female/male sterilization, lactation amenorrhea, and emergency contraception as modern methods (of note, rhythm and withdrawal are labeled in the DHS as traditional methods)[7,8]. The proportion of unmet need was defined in line with the definition of the WHO i.e. the gap between women's reproductive intentions and their actual contraceptive behavior.

The model simulated the natural history, specifically concerning sexual and reproductive health, of women in reproductive age, using cohorts of 100,000 women in both countries. In the analysis, the following four scenarios were evaluated: modern FP needs fulfilled by 25% (scenario 1), 50% (scenario 2), 75% (scenario 3) and 100% (scenario 4), while the comparator was defined as the current situation.

Modeled outcomes include clinical outcomes i.e. pregnancy and its subsequent potential consequences (e.g. live births, induced abortion, spontaneous abortions, and stillbirth), proportions of maternal mortality, costs of implementing the strategy, and ICERs of each scenario compared to the current situation.

The healthcare payer perspective was used, with only direct medical costs being considered. In the absence of country-specific guidelines, both long-term costs and health outcomes were discounted at 3%, a rate commonly used in many countries [9]. The primary outcome for the cost-effectiveness analysis was the ICER expressed per DALY averted. In the absence of country-specific willingness to pay (WTP) thresholds for Indonesia and Uganda (as well as for other L-MICs in general), we used a commonly used threshold for cost-effectiveness in L-MICs, defined in terms of the countries' per capita gross domestic products (GDPs), as described by WHO. The interventions would be considered very cost-effective if the value of the ICER per DALY averted was below the threshold of GDP per capita (US$ 3,492 for Indonesia and US$ 715 for Uganda), and still cost-effective if that value was below three times per capita GDP. Validation of the model was conducted including extreme value testing on transition probabilities, testing of model traces, as well as face validity testing on the conceptual model, input data, and model outcomes[10]. Deterministic and probabilistic sensitivity analyses were conducted to investigate the impact of model parameter uncertainty on cost-effectiveness results.

Model structure

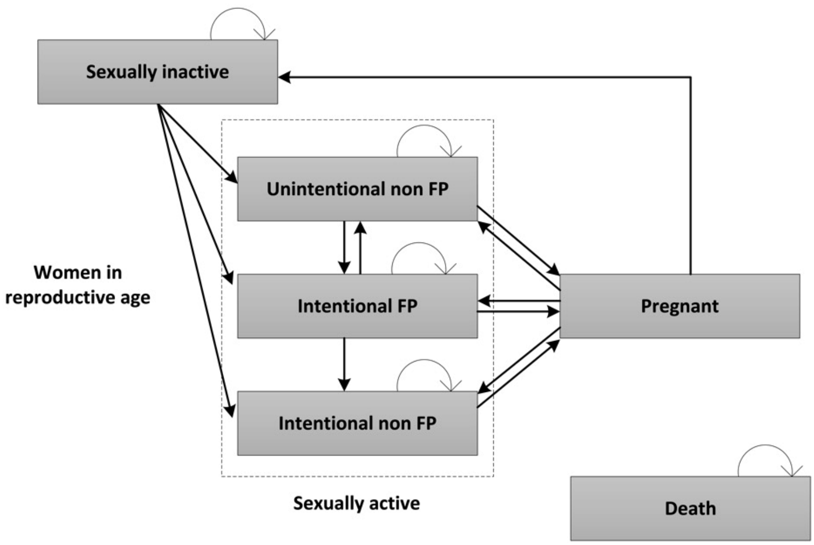
The schematic representation of the Markov model is provided in Figure 1. A hypothetical cohort of 100,000 15 until 49 years old women was followed over a time horizon of women's reproductive years, with age-group stratification based on DHS data[7,8]. The model has six health states that illustrate the various possible FP behaviors and transition probabilities that reflect the transfers between these various states.

Women in the reproductive age entered the model and were assigned a probability to be in the sexually inactive or in one of the sexually active states, i.e. (i) intentional FP, (ii) intentional non-FP, and (iii) unintentional non-FP. The details and assumptions for these states are explained below:

(i) Intentional FP represents women who use modern FP methods.

(ii) Intentional non-FP comprises women who consciously do not use any FP methods.

Unintentional non-FP indicates women who want to delay or cease fertility but do not use any FP methods or women with unmet need for FP.



The model simulates the various health states of sexual and reproductive health of women between 15-49 years old. All women start in the sexually inactive state and can either stay or transfer to any of the sexually active states before transitioning to the pregnant state. All women in each state may transition to death.
FP: (modern) family planning methods

Figure 1. Schematic structure of the Markov model.

Focusing on unmet need for modern FP methods, we assume users of traditional methods as having the unmet need[5]. Subsequently, all women in the sexually active states have a chance to get pregnant. Probabilities for pregnancies for both unintentional non-FP and intentional non-FP were assumed to be identical, representing probabilities of getting pregnant without any FP methods[11]. As the infecundity related to the start of the menopause will influence the chance of pregnancy, probabilities were adjusted using age-specific menopausal data[7,8]. In addition, annual discontinuation rates (Table 1) due to modern contraceptive failure were used to estimate the probabilities of pregnancy for women in the intentional FP state[7,8]. Although we defined the users of traditional methods as having the unmet need, we evaluated an alternative assumption regarding women using these methods in a sensitivity analysis.

In the absence of specific data, the probability to transition from unintentional non-FP to intentional FP was assumed to be equal as that from sexually inactive to intentional FP. Women in intentional FP could transition to either unintentional non-FP or intentional FP. The probabilities of the transition were estimated from annual discontinuation rates from the DHS. These probabilities were then adjusted to the proportions of different modern methods in both countries and assumed to be constant with age[7,8].

Once women are in the pregnant state, they can transition to either the sexually inactive state or any of the sexually active states (intentional FP, intentional non-FP, or unintentional non-FP). We used the assumption that women who exclusively breastfeed their infants (DHS chapter infant feeding) represent those who transition from pregnant to intentional FP, since the effectiveness of lactation amenorrhea as birth control was assumed to be similar to modern family planning methods[12,13]. We also assumed that the pregnant women who had outcomes other than live birth would make a transition to either unintentional non-FP or intentional non-FP, distributed over these two states similarly as done for the sexually inactive women.

Women in each health state could transition to the death state. The probabilities of dying were differentiated into death due to maternal complications and death due to other causes. The age-specific death rates from the WHO life tables were used to estimate the probabilities of death due to other causes, while the probability of death due to maternal complications was derived from the specific maternal mortality rate[7,8].

The cycle time for this model was nine months, as it reflects the pregnancy period and also was assumed to sufficiently represent the relevant transitions between all health states with adequate detail[14]. Some transition probabilities were age-dependent; i.e. all transitions from the sexually inactive, unintentional non-FP, and intentional non-FP states as well as from all states to death. Table 1 summarizes the input parameters of our model.

Table 1. Input parameters

Parameter		Base case		Sensitivity range (deterministic)		Distribution (PSA)		Reference	
		Indonesia	Uganda	Indonesia	Uganda	Indonesia	Uganda	Indonesia	Uganda
Proportion (% per age group)									
Sexually active[a];	15 - 19	12.8	36.5	NA	NA	Dirichlet	Dirichlet	7	8
	20 - 24	59.6	82.8						
	25 - 29	84.6	90.8						
	30 - 34	89.4	87.1						
	35 - 39	90.3	84.5						
	40 - 44	86.5	80.4						
	45 - 49	80.8	63.1						
Intentional use of family planning[b];	15 - 19	6.2	6	4.65 - 7.75	4.50 - 7.50	Dirichlet	Dirichlet	7	8
	20 - 24	35.4	19.8	26.55 - 44.25	14.85 - 24.75				
	25 - 29	52.2	27.6	39.15 - 65.25	20.70 - 34.50				
	30 - 34	56.7	30	42.53 - 70.88	22.50 - 37.50				
	35 - 39	57.9	30.3	43.43 - 72.38	22.73 - 37.88				
	40 - 44	53.5	26.5	40.13 - 66.88	19.88 - 33.13				
	45 - 49	36.3	14.1	27.23 - 45.38	10.58 - 17.63				
Unmet need for family planning[c];	15 - 19	6.67	57.21	5.01 - 8.34	42.90 - 71.51	Dirichlet	Dirichlet	7	8
	20 - 24	8.31	43.53	6.23 - 10.39	32.64 - 54.41				
	25 - 29	8.73	39.27	6.55 - 10.92	29.46 - 49.09				
	30 - 34	9.49	39.34	7.12 - 11.86	29.51 - 49.18				
	35 - 39	10.99	37.53	8.25 - 13.74	28.15 - 46.92				
	40 - 44	14.46	33.81	10.85 - 18.08	25.36 - 42.26				
	45 - 49	15.28	24.42	11.46 - 19.10	18.32 - 30.53				
Rate (annually)									
Discontinuation due to:									
Method failure		1.5	6.3	1.13 - 1.88	4.73 - 7.88	Dirichlet	Dirichlet	7	8
Desire to conceive		5.1	7.5	3.83 - 6.38	5.63 - 9.38	Dirichlet	Dirichlet	7	8
Any other reason		27.1	42.6	20.33 - 33.88	31.95 - 53.25	Dirichlet	Dirichlet	7	8
Maternal mortality		0.0019	0.0078	0.0014 - 0.0024	0.0058 - 0.0097	Dirichlet	Dirichlet	7	8

Table 1. Input parameters (*continued*)

Parameter	Base case		Sensitivity range (deterministic)		Distribution (PSA)		Reference	
	Indonesia	Uganda	Indonesia	Uganda	Indonesia	Uganda	Indonesia	Uganda
Modern family planning methods (%)								
Oral contraceptives	23.00%	10.00%	NA	NA	NA	NA	7	8
Intrauterine devices	7.00%	2.00%					7	8
Injectables	55.00%	52.00%					7	8
Implants	6.00%	9.00%					7	8
Condoms	3.00%	16.00%					7	8
Female sterilization	6.00%	11%					7	8
Traditional family planning method (%)								
Overall traditional method	3%	4%	NA	NA	NA	NA	7	8
Pregnancy outcomes (%)								
Induced abortion	1.30%	19.00%	NA	NA	NA	NA	33	14
Spontaneous abortion	4.30%	4.90%					34	14
Vaginal live birth	76.00%	61.50%					7	14
Cesaeran live birth	10.40%	11.50%					35	14
Stillbirth	0.20%	2.40%					7	14
DALYs lost								
Maternal complications	0.35	0.27	0.26 - 0.43	0.20 - 0.34	Beta	Beta	16,17	14
Costs (US$)								
Intentional family planning	20.91	20.21	10.46 - 31.37	10.10 - 30.31	Gamma	Gamma	7,17	8,14
Pregnancy	182.78	101.4	91.39 - 274.18	50.70 - 152.09	Gamma	Gamma	17,33-35	8,14,19,36
Discount rates								
Costs	3%	3%	0% - 5%	0% - 5%	NA	NA	Assumption	Assumption
Outcomes	3%	3%	0% - 5%	0% - 5%	NA	NA	Assumption	Assumption

DALY: disability adjusted life years, NA: Not applicable, PSA: Probabilistic sensitivity analysis

[a] Age-specific proportions of sexually active women were used to adjust the probability of women from sexually inactive state to sexually active state in the model (details on Supplementary material)

[b] Proportions of intentional use of family planning were used to weigh the transition probability from sexually inactive state to intentional FP.

[c] Proportions of unmet need for family planning were used to weigh the transition probability from sexually inactive state to unintentional non-FP.

Data sources

Transition Probabilities

State-transition probabilities were estimated from the DHS and published studies (see Table 1). Because straightforward data estimates on incidence of sexually active women in their reproductive years were not available, we adapted the approach proposed by van de Kassteele et al [15] for estimating transitions from the sexually inactive to sexually active state.

All estimates in this section were adequately converted to transition probabilities conform the cycle length of the Markov model (i.e. nine months). Details on transition probabilities and how they were derived are provided in Supplementary material S1.

Health outcomes

The country-specific number of DALYs associated with maternal causes was derived from the WHO Global Burden of Disease (GBD) study. Loss of DALYs for both countries was estimated by weighting the estimated DALYs per pregnancy with the average number of pregnancies [14,16]. In the WHO GBD study, the average DALY loss due to maternal complications per pregnancy was estimated to be 0.346 and 0.272 for Indonesia and Uganda, respectively, reflecting the average for women in the reproductive age (15-49 years old) [17].

Costs

Costs were estimated only for intentional FP and the pregnant state. We assumed that the other states were not associated with any costs. Direct medical costs for intentional FP include costs of various FP methods that were weighted by their country-specific proportions of use and costs of healthcare personnel. Selected costs for pregnancy include costs of healthcare personnel, materials and devices for antenatal care and costs of the several distinguished potential pregnancy outcomes, i.e. induced abortion, spontaneous abortions, vaginal live birth, caesarean live birth, stillbirth and maternal complications. The country-specific proportions of these potential outcomes were used to estimate the overall pregnancy costs. For Indonesia, official tariffs from public access government databases were used [18] to estimate the costs. For Uganda, we applied cost estimations from published articles[14,19,20]. All costs were converted to 2015 US Dollar (USD) using inflation rates from the World Bank and official exchange rates from the World Bank annual consumer index. Further details on health outcome measures and costs are provided in Supplementary material S2 and S3.

Sensitivity analysis

Deterministic and probabilistic sensitivity analyses were performed to determine which parameters substantially influence the outcomes and to assess the uncertainty in the model parameters. In the deterministic analysis, one-way sensitivity analysis was performed, with several relevant parameters in the model being varied in ranges of plausible values. All parameters were varied using 95% confidence intervals where available and, if unavailable, plus-minus 25% for transition probabilities and DALYs lost and plus-minus 50% for costs[14]. The ranges used for the sensitivity analysis are listed in Table 1.

In probabilistic sensitivity analysis, all parameters were varied simultaneously within their respective probability distributions. Monte Carlo simulation was used to create 1,000 iterations for which the expected outcomes were calculated. Dirichlet distributions were fitted for probabilities (because the data were multinomial), beta distributions for DALYs and gamma distributions were used for costs, using predefined standard errors.

RESULTS

Base case

Model validation

Extreme value testing on transition probabilities resulted in reasonable outcomes within the model. Testing of traces where women in the entire cohort were tracked through the model to determine its logic, resulted in logical outcomes as well. The face validity of the model outcomes was assessed by comparing the results to the data from the DHS. The model estimates of maternal mortality rate, i.e. 0.23 for Indonesia and 1.26 for Uganda, expressed per 1,000 woman-years of exposure, closely approximated the DHS estimations of 0.21 and 0.93 for Indonesia and Uganda, respectively.

Clinical outcomes

In the hypothetical cohort of 100,000 women, fulfilling the unmet need for family planning resulted in a reduction of unintended pregnancies ranging from 2,483 to 9,597 fewer pregnancies in Indonesia, and 15,888 to 52,014 fewer pregnancies in Uganda, over the range of the four scenarios investigated. Also, it resulted in fewer maternal-related adverse events such as induced abortions, spontaneous abortions, and stillbirths. Maternal mortality was also lower in the scenarios, with a reduction of 2.07% to 3.05% in Indonesia and 2.09 % to 6.83% in Uganda, corresponding with reductions per 1,000 woman-years of exposure of 0.23 to 0.20 and 1.26 to 0.98, respectively. Table 2 presents the total number of events of maternal morbidity and mortality for the intervention scenarios as compared to the current situation.

Table 2. Cohort clinical outcomes per 100,000 women

	Indonesia		Uganda	
	Total events	**Difference**[a]	**Total events**	**Difference**[a]
Current situation				
Total pregnancies	563,300		777,909	
Vaginal live birth	427,922		478,414	
Caesarean live birth	58,809		89,460	
Induced abortions	7,121		147,803	
Spontaneous abortion	24,222		38,118	
Stillbirth	1,189		18,670	
Maternal death	820		4,425	
Scenario 1 (Modern FP needs fulfilled by 25%)				
Total pregnancies	560,817	-2,483	765,451	-12,458
Vaginal live birth	426,036	-1,886	470,752	-7,662
Caesarean live birth	58,549	-206	88,027	-1,433
Induced abortions	7,090	-25	145,436	-2,367
Spontaneous abortion	24,115	-86	37,507	-610
Stillbirth	1,184	-4	18,371	-299
Maternal death	803	-17	4,333	-92
Scenario 2 (Modern FP needs fulfilled by 50%)				
Total pregnancies	558,391	-4,909	754,368	-23,541
Vaginal live birth	424,193	-3,729	463,936	-14,477
Caesarean live birth	58,296	-409	86,752	-2,707
Induced abortions	7,059	-50	143,330	-4,473
Spontaneous abortion	24,011	-171	36,964	-1,153
Stillbirth	1,179	-8	18,105	-565
Maternal death	800	-20	4,251	-174
Scenario 3 (Modern FP needs fulfilled by 75%)				
Total pregnancies	556,021	-7,280	744,262	-33,647
Vaginal live birth	422,392	-5,530	457,721	-20,693
Caesarean live birth	57,807	-608	85,590	-3,869
Induced abortions	7,029	-75	141,410	-6,393
Spontaneous abortion	23,909	-256	36,469	-1,649
Stillbirth	1,174	-13	17,862	-808
Maternal death	797	-22	4,178	-247
Scenario 4 (Modern FP needs fulfilled by 100%)				
Total pregnancies	553,703	-9,597	734,880	-43,029
Vaginal live birth	420,632	-7,290	451,951	-26,463
Caesarean live birth	59,500	-804	84,511	-4,948
Induced abortions	7,000	-99	139,627	-8,176
Spontaneous abortion	23,809	-339	36,009	-2,108
Stillbirth	1,169	-17	17,637	-1,033
Maternal death	795	-25	4,123	-302

[a] Compared to the current situation
Clinical outcomes were estimated by weighting the respective proportion to the estimated number of pregnancies from the model.

Costs and cost-effectiveness

The summary of total costs and effectiveness results is provided in Table 3. Overall, total costs of the interventions were lower than the current situation in both Indonesia and Uganda. From a healthcare payer perspective, fulfilling the unmet need for family planning in a hypothetical cohort of 100,000 women of reproductive age resulted in savings within a range of US$ 230,613 to US$ 893,111 in Indonesia and US$ 564,386 to US$ 1,865,873 in Uganda.

Total DALYs were also lower in all scenarios compared to the current situation for both countries, with reductions ranging from 1,859 to 3,780 and 3,705 to 12,230 in Indonesia and Uganda, respectively. Both monetary savings and DALY reductions indicated that the scaling up was most beneficial in a country with high unmet need such as Uganda.
As all scenarios of improved FP were both cost saving and more effective i.e. dominant, formal calculation of ICERs appeared irrelevant in the base case. The dominance of all scenarios over the current situation suggests that improved FP is highly recommendable from a health economic perspective in both countries considered.

Table 3. Total costs and effectiveness results for 100,000 women (formal ICERs not indicated as dominance exists for all scenarios in both countries)

	Total cost (US$)	Total DALYs
Indonesia		
Current situation	89,347,424	120,306
Scenario 1	89,116,811	118,448
Scenario 2	88,891,199	117,793
Scenario 3	88,670,420	117,153
Scenario 4	88,454,313	116,526
Uganda		
Current situation	68,325,400	135,579
Scenario 1	67,761,014	131,873
Scenario 2	67,259,122	128,582
Scenario 3	66,809,744	125,639
Scenario 4	66,459,526	123,348

DALY: Disability adjusted life year
ICER: Incremental cost-effectiveness ratio

Sensitivity analysis

The tornado diagrams for the deterministic sensitivity analysis are presented in supplementary material S4. In the deterministic sensitivity analysis, discount rates seem to be the most influential variable for both costs and DALYs. Other variables that also importantly influence the costs concerned the cost of pregnancy and that of family planning, while uncertainty in DALYs lost due to maternal complications and discontinuation rate on modern contraceptives were the parameters to which DALYs appeared most sensitive. In Indonesia, when cost of family planning and pregnancy were reduced, the intervention appeared to be more costly although it remained more effective. The ICERs that were observed ranged from US$ 3337 – US$ 1466 and US$ 8433 – US$ 3971 per DALY averted, and the same trend was also observed in Uganda, at ICER ranging from US$ 1047 – US$ 211 and US$ 3257 – US$ 880 per DALY averted, for lower cost of family planning and pregnancy, respectively. Variation in the proportion of unmet need, the menopausal rate and the pregnancy rate in traditional FP methods seemed to be less influential for both costs and DALYs.

Results from the probabilistic sensitivity analysis are presented in Figure 2 and Figure 3 with a similar trend depicted in both Indonesia and Uganda. Specifically, the majorities of simulations show consistent cost-savings. Yet, some uncertainty remains, with a possibility that scenarios to reduce the unmet need for family planning would be more costly than current situation; notably 8.43% and 7.75% of simulations in Indonesia and Uganda, respectively. At WTP thresholds of both once and three times GDP per capita, it was 100% certain that the interventions would be cost-effective. The cost-effectiveness acceptability curves, which show the probability for each scenario to be cost-effective, are presented in Supplementary material S5.

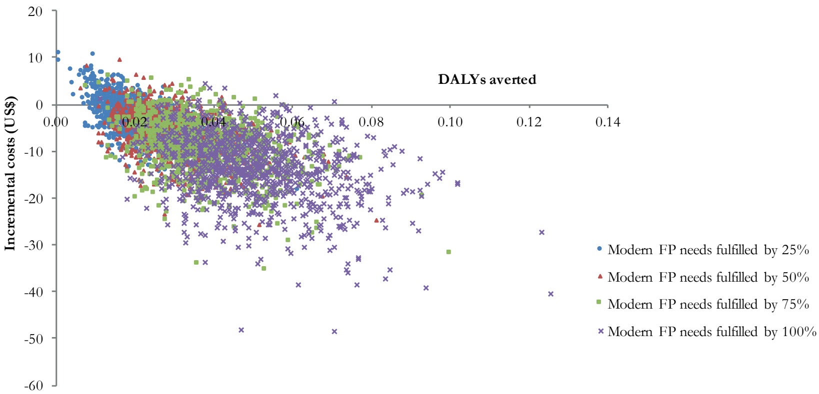


Figure 2. Scatter plot of incremental costs and effects compared to the current situation obtained from probabilistic sensitivity analysis in Indonesia

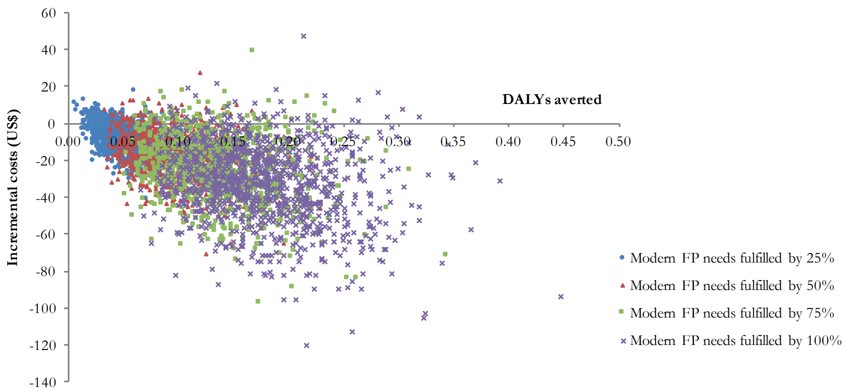


Figure 3. Scatter plot of incremental costs and effects compared to the current situation obtained from probabilistic sensitivity analysis in Uganda

DISCUSSION

Our study suggests that scaling up modern FP interventions in L-MICs, particularly Indonesia and Uganda, results in considerable reductions of maternal morbidity and mortality along with substantial monetary savings for both countries. Additionally, our results suggest that this finding might apply to both countries with relatively low unmet need for modern FP such as Indonesia, as well as to countries with low modern contraceptive use and high unmet need, such as Uganda. Notably, the most favorable findings were observed in a setting with higher unmet need. This trend is expected, considering that countries with higher unmet need would benefit more from the scaled-up interventions, as in absolute terms there is more to gain here. Furthermore, the results remain consistent under deterministic and probabilistic sensitivity analyses, suggesting that these findings are robust.

The perceived importance of improving FP interventions in L-MICs is sometimes hampered by the lack of comprehensive understanding of the potential real benefits in terms of both costs and health consequences for the local policy-makers. In addition to being cost saving or at least cost-effective, integrating the interventions for scaled-up FP has previously been shown to be both an efficient and feasible way to reduce the number of unintended pregnancies and also maternal mortality. To date, there have been limited studies focusing on economic evaluation of FP interventions in L-MICs. Nevertheless, our finding is consistent with previous research in other L-MICs suggesting that the initiative to improve FP interventions in order to decrease the unmet need is economically favorable[6,21,22]. Previous studies in Uganda analyzed that the scenario to promote universal access to modern contraceptives dominates the current situation with reduced costs and less DALYs[14], while another study showed that reducing the unmet need for Ugandan women would result in savings of approximately $3 per every dollar spent, while it also resulted in reduced maternal mortality and less induced abortions[23]. Studies in Mexico[24], India[25], Afghanistan[26], and Nigeria[27] suggested that early intensive effort to improve FP is the most cost-effective single intervention to reduce maternal mortality and morbidity. No previous studies exist for Indonesia.

A study on reproductive, maternal, newborn, and child health, as part of a broader consideration of health priorities, estimated that the average cost of eliminating all unmet needs in L-MICs for effective family planning would involve costs for approximately 209 million additional contraception users, at an average cost of $13.9 per new user ($15.8, $10.0, and $24.4 in low-income, lower-middle-income, and in upper-middle-income country groups, respectively)[21]. Based on the conclusion from this broader study as well as results from previous studies, the cost required for the additional users can be offset by the potential health benefits and burden averted. The study also suggested that reproductive and deaths related to maternal complications could most substantially be reduced by scaling up the most economically-favorable integrated interventions, especially FP as well as labor and delivery management[21]. Nonetheless, country-specific implementation research is necessary to adapt these interventions to the local health service context in order to achieve more specific estimations of strategies. As such, the findings from our study complement scarce other country-specific studies for the specific estimation of the potential cost-effectiveness of scaling up FP interventions in L-MICs.

Our study has some limitations. Notably, our estimations depended on the available underlying evidence with volatile quality and completeness. For instance, there were discrepancies between both countries in the definitions of current use of contraceptives in the DHS. In Uganda, the distribution of women who use specific FP methods included all women, irrespective of their marital status[8]. However, according to the Indonesian DHS, since only very few unmarried women reported current use of contraception, the data focused only on currently married women[7]. As a consequence, we may have underestimated the use of contraceptives in Indonesia and overestimated the total number of pregnancies, as reflected in the estimation of total pregnancies and fertility rate. Yet, the pregnancy rate as predicted by the model for Uganda closely approximated the fertility rate as reported in the DHS. The likely under-reporting of induced abortion, including self-induced abortions, especially in Indonesia, reflects a limitation in our estimation. Induced abortion is highly restricted and a very sensitive topic, therefore accurate data sources are limited and difficult to obtain. It was previously estimated that in Indonesia, 37 abortions per 1,000 women of reproductive age occurred annually[28], however the number of spontaneous abortions was also included in this estimation. We think that using the DHS-data as the source for this analysis is the best way to ensure consistency within and between countries. However, because the DHS is self-reported, its limitations should be kept in mind in interpreting the results of the model, especially where it concerns a sensitive issue like induced abortions. As a consequence of the fact that we have no data on the number of self-induced abortions, we also could not capture the associated morbidity and mortality with these abortions, implying that current model estimates are conservative in this respect, and true health gains and cost savings could be even higher than estimated here.

Ideally, estimations are derived straightforwardly when individual-based risk factors can be captured from clinical trials or large cohort studies[15,29]. However, some of our estimates for transition probabilities were derived

from transforming age-specific prevalence data into transition probabilities, because such data on risk-factors or incidence were not available.
Next, we may have underestimated the economic attractiveness in our scenarios because we only considered the direct medical costs and ignored possible out-of-pocket expenses and indirect costs such as those of productivity losses. The inclusion of these costs would likely result in a more favorable cost-effectiveness, due to greater monetary savings as a result from extra cost being included in our estimate of total pregnancy cost, as shown in a previous study in Uganda[14]. Finally, we note that our model was directed at maternal complications only, whereas inclusion of complications in the children such as prematurity and low birth weight could have further strengthened our results. However, in the absence of such evidence, we could only perform the analysis from our current more limited perspective.
The UN Millennium Development Goals (MDG) put family planning high on the development agenda. Improving maternal health was one of the 8 MDG goals, and contraceptive prevalence rate and unmet need of FP were two key indicators used to measure its progress[30,31]. The UN Sustainable Development Goals (SDG), launched in 2016, specify 17 goals, with among them highlighted universal access to sexual and reproductive health-care services, including family planning[32] . In order to achieve these goals, interventions in reproductive, maternal, and child health should be a priority and be seen as an integrated care approach. Future studies should further contribute to these goals by taking into account the contribution of scaled up FP interventions along with other interventions in maternal and child health and measure potential health benefits not only for the mothers, but also for the offspring.
In conclusion, scaling up modern FP interventions in two selected L-MICs appears to be dominant or at least very cost-effective in all scenarios and sensitivity analyses examined, compared to the current situation. Furthermore, countries with a low rate of modern contraceptive use and a high unmet need would benefit the most from the scaled-up intervention. Interventions to reduce the unmet need for FP should be considered as an economically highly attractive way to address this important issue on the global health agenda, i.e. to improve women's and maternal health.

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SUPPLEMENTARY MATERIALS

S1. Transition probabilities

Transition probability from sexually inactive to sexually active

The country-specific probabilities from the sexually inactive state to any of the sexually active states were estimated age-dependently with five-year intervals based on the empirical frequencies of sexual intercourse reported among women aged 15-49[1,2] specified in Table S1.2. The initial prevalence proportions for sexually inactive and sexually active were estimated by fitting logistic regression models to the frequencies of being sexually inactive and sexually active with the median age from each subgroup as the model covariate. These frequencies were captured based on the aforementioned reported frequencies of sexual intercourse. Subsequently, the probability of remaining in the sexually inactive state was estimated based on adapting the general framework specified by van de Kassteele et al[3]. The transition probabilities from the sexually inactive state to any of the sexually active states were then estimated by one minus the corresponding remaining probabilities. The age-specific transition probabilities were assumed to remain stable over time. All probabilities within the sexually active states were estimated by weighting the probabilities with their respective proportion.

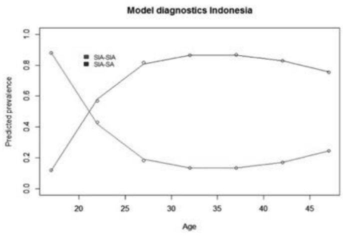
Based on van de Kassteele et al[3], the relationship between estimated prevalence proportions and the transition probabilities can be described in a general formula as follows:

$$\sum_{i=1}^{k} P'_{ij}(a) = \frac{\widehat{\pi_j}(a)}{\widehat{\pi_i}(a-1)}$$

where *k* denotes the number of states, *i* and *j* denote the index of the specific state, *a* denotes the specific age group and $\widehat{\pi_j}(a)$ and $\widehat{\pi_i}(a-1)$ specifically denote the estimated prevalence proportions for the current age group and the previous age group. In our study, we focused on the estimation of the remaining probability in one specific health state (so we have the situation that k=1 and i=j=1). Hence, in our case, the general formula reduced to the more straightforward form as follows:

$$P'(a) = \begin{cases} \hat{\pi}(a), if\ a\ is\ the\ first\ age\ group \\ \dfrac{\hat{\pi}(a)}{\hat{\pi}(a-1)}, if\ \hat{\pi}(a) < \hat{\pi}(a-1) \\ 1, otherwise \end{cases}$$

Figure S1.1. Estimated prevalence proportions from logistic regression model for Indonesia and Uganda



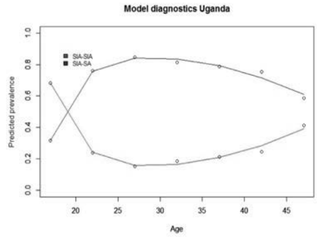
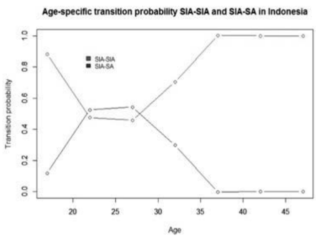
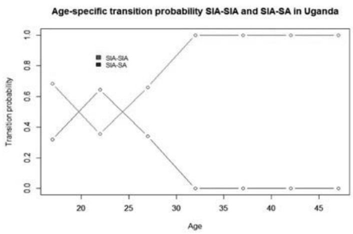


Figure S1.2. Estimated age-specific transition probabilities from sexually inactive to any of sexually active states in Indonesia and Uganda





SA: Sexually active
SIA: Sexually inactive

Table S1.1. Non age-specific transition probabilities used in base-case analysis

Parameters	Probabilities			
	Current situation		Sensitivity range[1]	
	Indonesia	Uganda	Indonesia	Uganda
IFP - INFP	0.038	0.055	0.028 - 0.047	0.041 - 0.068
IFP - UNFP	0.184	0.273	0.141 - 0.224	0.213 - 0.329
IFP - PRE	0.011	0.046	0.008 - 0.014	0.035 - 0.057
PRE - SIA	0.108	0.073	NA	NA
PRE - IFP	0.756	0.657	NA	NA
PRE - UNFP	0.018	0.085	NA	NA
PRE - Death[2]	0.0014	0.0058	0.00108 - 0.00180	0.00435 - 0.00544

IFP: intentional family planning, INFP: intentional non-family planning, UNFP: unintentional family planning, PRE: pregnant, SIA: sexually inactive
NA: not applicable
[1]As applied in deterministic sensitivity analysis
[2]Referred as probability of maternal death

Table S1.2. Distribution of women age 15-49 by timing of last sexual intercourse in Indonesia and Uganda[1,2]

Age group	**Timing of last sexual intercourse**								**Never had sexual intercourse**		**Total[b]**	
	Within the past 4 weeks		Within 1 year[a]		One or more years		Missing					
	IND	UG	IND	UG	IND	UG	IND	UG	IND	UG	IND	UG
15-19	707	383	887	748	55	176	14	0	5971	1124	6927	2048
20-24	3089	938	3764	1349	151	145	19	2	2371	134	6305	1629
25-29	5010	1054	5887	1425	313	129	35	3	724	13	6959	1569
30-34	5274	708	6147	946	378	129	41	2	309	9	6876	1086
35-39	5196	633	6221	867	420	155	28	2	213	2	6882	1026
40-44	4395	449	5408	586	656	141	56	1	131	0	6252	729
45-49	3179	262	4369	370	887	212	49	5	103	0	5407	587

IND: Indonesia UG: Uganda

[a] Includes women who had sexual intercourse within the last 4 weeks

[b] Total of reproductive age women that included in the survey

Table S1.3 Age-specific transition probabilities used in base-case analysis

Parameters	**15-19**		**20-24**		**25-29**		**30-34**		**35-39**		**40-44**		**45-49**	
	IND	UG	IND	UG	IND	UG	IND	UG	IND	UG	IND	UG	IND	UG
SIA - UNFP	0.008	0.182	0.044	0.280	0.047	0.134	0.028	0.000	0.000	0.000	0.000	0.000	0.000	0.000
SIA/UNFP - IFP	0.008	0.019	0.186	0.128	0.283	0.094	0.168	0.000	0.000	0.000	0.000	0.000	0.000	0.000
SIA - SIA	0.882	0.682	0.475	0.356	0.458	0.660	0.702	0.995	0.999	0.994	0.998	0.993	0.997	0.992
UN/INFP - PRE	0.638	0.638	0.638	0.638	0.638	0.638	0.565	0.621	0.551	0.612	0.530	0.570	0.415	0.548
UN/INFP – PRE (TRA¶)	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200
All states - death*	0.0005	0.0022	0.0007	0.0029	0.0008	0.0042	0.0010	0.0052	0.0013	0.0064	0.0018	0.0072	0.0028	0.0077

IND: Indonesia, UG: Uganda

¶ Probability of pregnancy after adjusted to the probability of pregnancy for women using traditional family planning methods weighted by its country-specific proportion

*All states excluding pregnant state

S2. Health outcomes measure

Disability adjusted life years averted

Incremental clinical outcome (morbidity and mortality) was compared between the current situation and each scenario. DALYs due to maternal complications were derived from WHO Global Burden of Disease and estimated as follows:

DALYs for a disease or health condition were calculated as the sum of years of life lost due to premature mortality (YLL) and disability (YLD). The years of life lost (YLL) corresponded to the number of deaths multiplied by the standard life expectancy at the age at which death occurred. The basic formula for YLL (gender and age specific and for a given cause):

YLL = N x L

N = number of deaths

L = standard life expectancy at age of death in years

In order to estimate YLD for a given cause in a particular time period, the number of incident cases was multiplied by the average duration of the disease and disability weight which was on a scale from 0 (perfect health) to 1 (dead). The basic formula for YLD:

YLD = I x DW x L

I = number of incident cases

DW = disability weight

L = average duration of the case until remission or death (years)

In estimating DALYs, the WHO Global Burden of Disease Study excluded non-health characteristics such as race and socioeconomic status and applied a 3% time discounting[4].

S3. Costs

Intentional family planning

The proportion of women who use modern family planning methods was derived from the DHS, chapter family planning[1,2]. Unit costs for every method were estimated from both survey and previously published studies[1,2,5]

Table S3.1. Costs and proportion of women who use modern family planning methods

Item	Proportion		Unit costs (US$)		Adjusted costs (US$)	
	IND	UG	IND	UG	IND	UG
Oral contraceptives	23%	10%	0,5	6,6	0,1	0,7
Intrauterine devices (IUD)	7%	2%	12,2	1,8	0,9	0,0
Injectables	55%	52%	1,8	5,9	1,0	3,1
Implants	6%	9%	10,2	37,6	0,6	3,5
Condoms	3%	16%	0,8	6,2	0,0	1,0
Female sterilization	6%	11%	238,7	5,4	14,0	0,6
Total (US$)					16.6	8.9

Total costs of intentional family planning included costs for the methods and healthcare personnel. Based on standard national tariffs from the Ministry of Health in Indonesia[6], we assumed that only IUD, injectables, and sterilization included personnel costs. For Uganda, a previously published study was used to estimate personnel costs, and it was assumed that personnel costs were applied for all methods[5] . Furthermore, it was assumed that the number of visits per cycle was three, except for long-term methods, which were assigned one visit per cycle.

Table S3.2. Healthcare personnel costs of intentional family planning

Item	Type	Visit/ cycle	Unit costs (US$)*		Adjusted costs (US$)	
			IND	UG	IND	UG
Oral contraceptives	Short-term	3	0.0	3.8	0.0	11.4
Intrauterine devices	Long-term	1	0.6		0.6	
Injectables	Short-term	3	0.7		2.1	
Implants	Long-term	1	0		0.0	
Condoms	Short-term	3	0		0.0	
Female sterilization	Long-term	1	1.7		1.7	
Total (US$)					4.4	11.4

*Unit costs (Indonesia) after adjustment to their proportion

Pregnancy

The proportion of each potential pregnancy outcome, i.e termination, miscarriage, vaginal live birth, caesarean live birth, stillbirth and maternal complications, was used to estimate the overall average pregnancy costs. Antenatal cost was assumed to be generated exclusively by visits to the midwife at an average total of 3 visits per pregnancy.

Table S3.3. Pregnancy costs

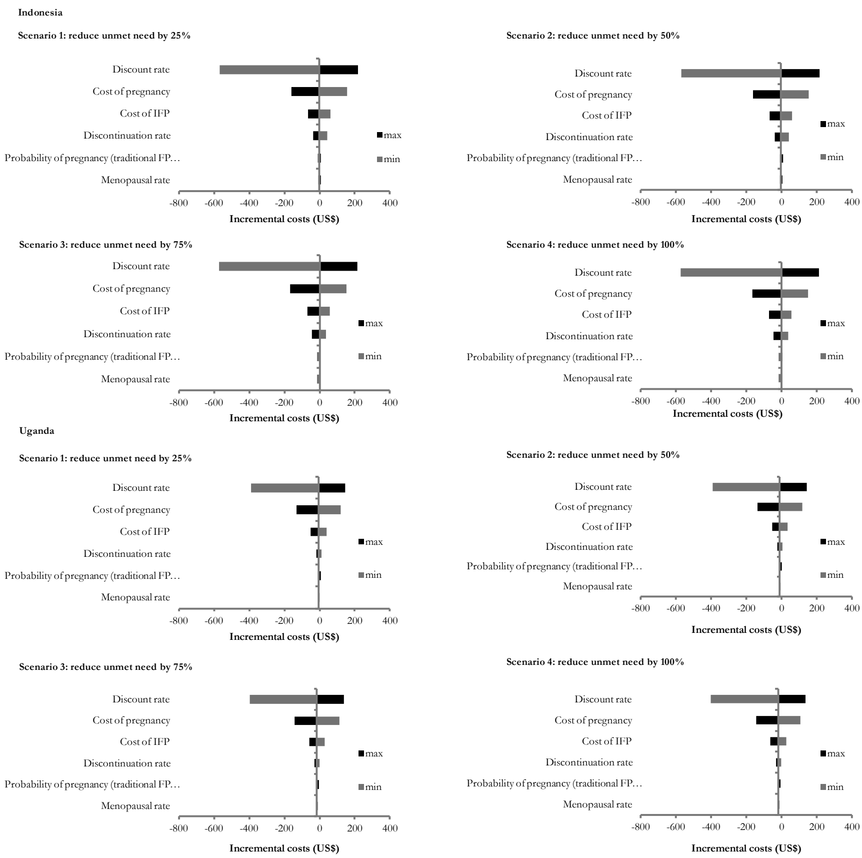
Pregnancy outcome	Proportion		Unit costs (US$)*		Adjusted costs (US$)		Ref	
	IND	UG	IND	UG	IND	UG	IND	UG
Antenatal care	96.0%	96.0%	2.1	9.8	6.1	28.2	1	2
Termination	1.3%	19.0%	476.4	86.1	6.0	16,4	7	8
Miscarriage	4.3%	4.9%	183.4	86.1	7.9	4,2	9	5
Vaginal live birth	76.0%	61.5%	106.7	46.2	81.1	28,4	1	5
Cesaeran live birth	10.4%	11.5%	538.2	173.8	56.2	20,0	10	5
Stillbirth	0.2%	2.4%	489.8	110.0	1.0	2,6	1	5
Complications	7.8%	0.7%	313.6	221.9	24.5	1,6	7	11
Total (US$)					182.8	101.4		

*Unit costs included both healthcare personnel and healthcare material

S4. Deterministic sensitivity analysis

The effect of uncertainty in different parameters between scenarios and current situation on 1) incremental costs 2) incremental DALYs in Indonesia and Uganda

1)

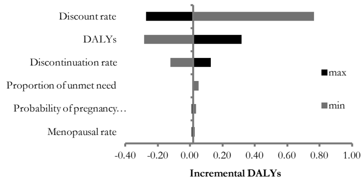


IFP: intentional family planning

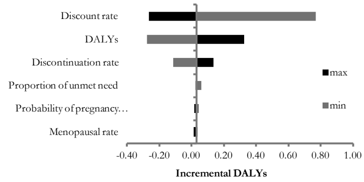
2)

Indonesia

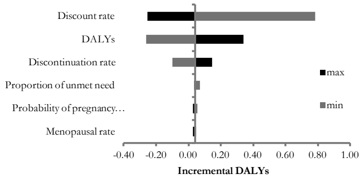
Scenario 1: reduce unmet need by 25%



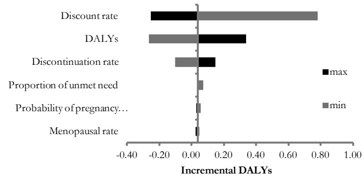
Scenario 2: reduce unmet need by 50%



Scenario 3: reduce unmet need by 75%

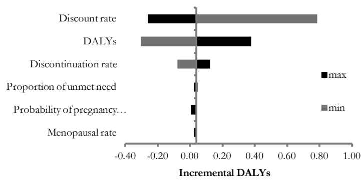


Scenario 4: reduce unmet need by 100%

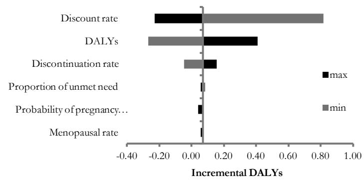


Uganda

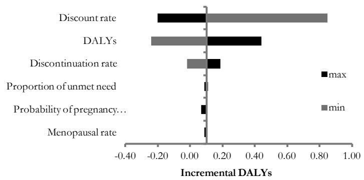
Scenario 1: reduce unmet need by 25%



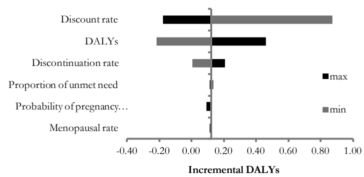
Scenario 2: reduce unmet need by 50%



Scenario 3: reduce unmet need by 75%

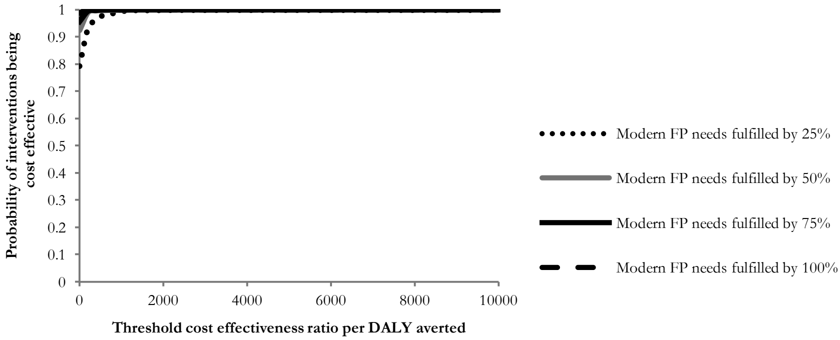


Scenario 4: reduce unmet need by 100%

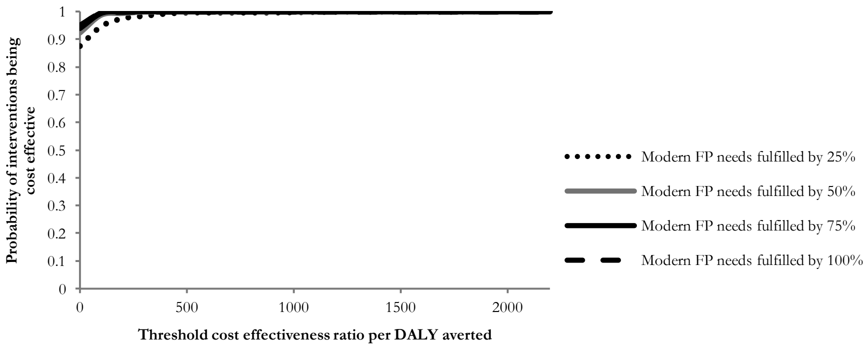


S5. Cost-effectiveness acceptability curves (CEAC)

Indonesia:



Uganda:



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SECTION II

MATERNAL HEALTH